Supplementary Online Material

Figure S1. ICP-DRC-MS shows no significant changes in the levels of zinc, copper or manganese in proteasome degradation-defective *Mtb*. ICP-DRC-MS results for (A) zinc, (B) copper, and (C) manganese. 10 ml of *Mtb* cultures were grown in 7H9 to early stationary phase, lysed in nitric acid, neutralized and brought up to 3 ml in metal free water. After ICP-DRC-MS analysis, we calculated the number of atoms per CFU. Data are representative of three replicates.

Figure S2. *socAB* is expressed in *Mtb*. WT *Mtb* RNA was used as a template for cDNA synthesis using random hexamers to prime the reaction following the same protocol used for cDNA preparation for qRT-PCR. cDNA was used as a template for PCR. Lanes correspond to samples treated with RT (+), without RT (-) or samples using genomic DNA as a positive control for the PCR (G). Shaded bars correspond to the amplified fragments.

Figure S3. *ctpV* does not respond to copper in the Δ*csoR::hyg* mutant. *ctpV* RNA levels in WT *Mtb* and the Δ*csoR::hyg* mutant with and without copper were measured using qRTPCR. This is representative of two biological replicates, done in triplicate.

Figure S4. *Mtb* copper sensitivity is dose dependent. We performed a copper sensitivity assay as described in Fig. 6 and in the *Experimental Procedures*. The OD_{580}

was measured after 10 days of exposure to varying levels of $CuSO_4$ added to Sauton's minimal media.

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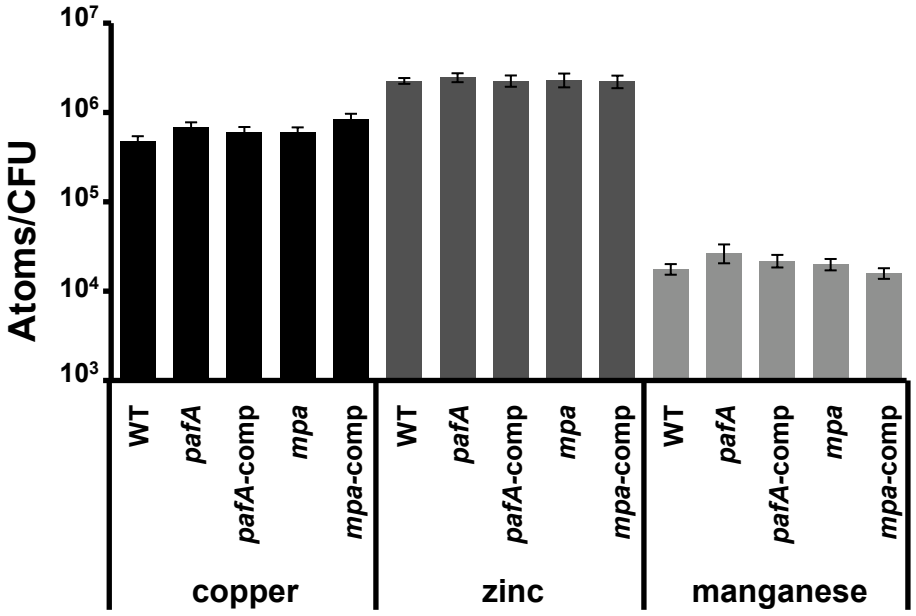
Supplemental Figure 1



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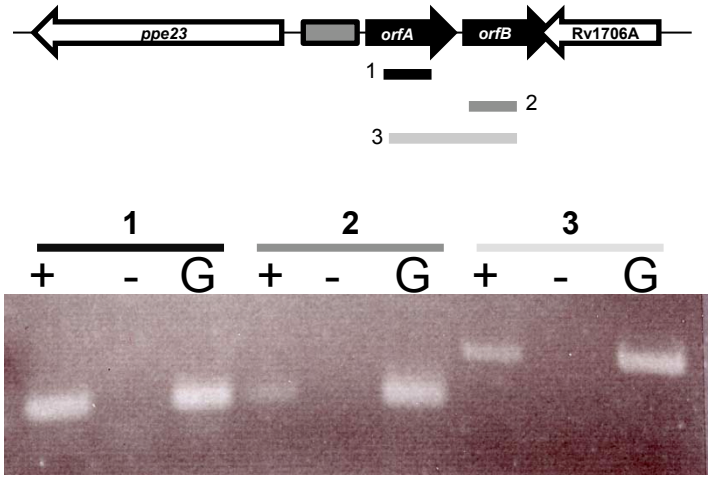
Supplemental Figure 2



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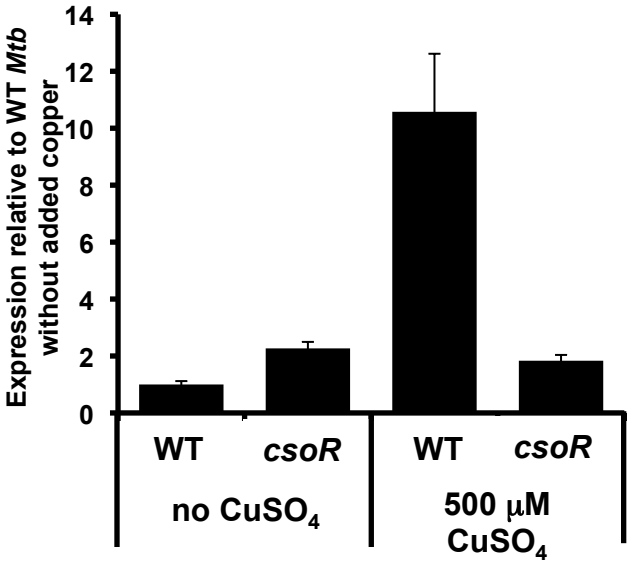
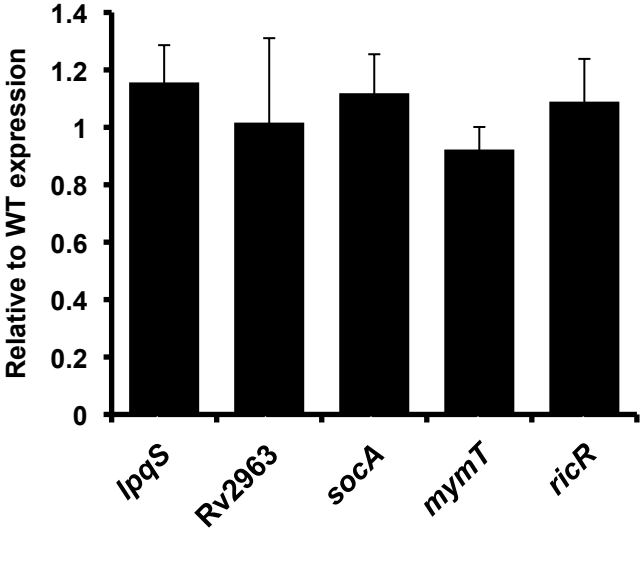
Supplemental Figure 3

A.



B.



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Supplemental Figure 4

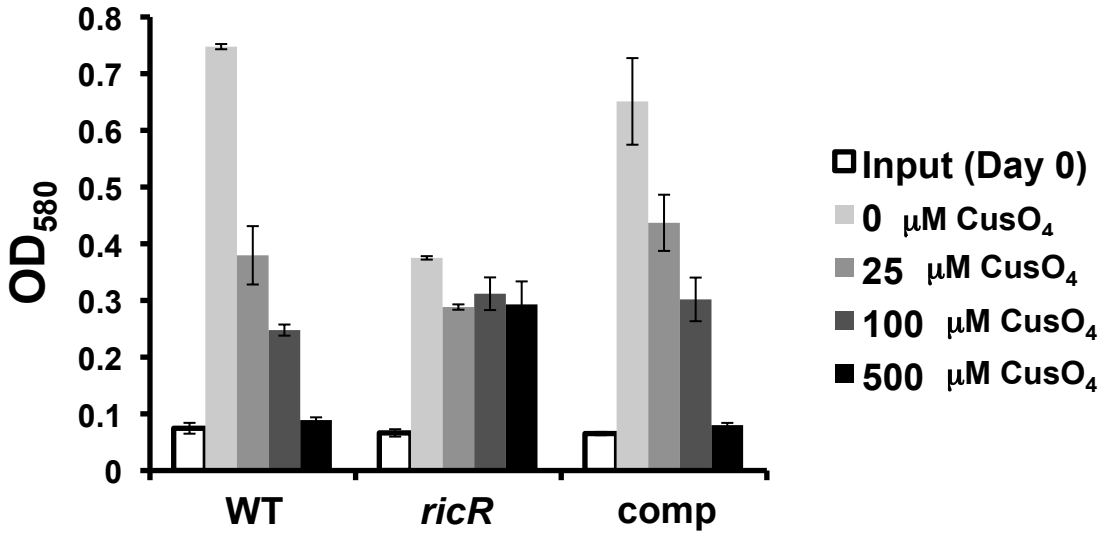

Table S1. Strains, Plasmids and Primers

Strain, plasmid, or primer	Genotype or sequence	Source or Reference
***M. tuberculosis* strains:**		
H37Rv:		
H37Rv	WT	American Type Culture Collection 25618
MHD2	Kan^R; *pafA::*ΦMycoMarT7	(Darwin et al., 2003)
MHD4	Kan^R; *mpa607::*ΦMycoMarT7	(Darwin et al., 2003)
MHD5	Kan^R; *mpa::*ΦMycoMarT7	(Darwin et al., 2003)
MHD18	Hyg^R; WT, pMV306, Strain:H37Rv	(Darwin et al., 2003)
MHD22	Kan^R, Hyg^R; *mpa::*ΦMycoMarT7, pMV306	(Darwin et al., 2003)
MHD23	Kan^R, Hyg^R; mpa::FMycoMarT7, pMV306-mpa	(Darwin et al., 2003)
MHD62	Kan^R, Hyg^R; *pafA::*ΦMycoMarT7, pMV306	(Festa et al., 2007)
MHD63	Kan^R, Hyg^R; *pafA::*ΦMycoMarT7, pMV306	(Festa et al., 2007)
MHD572	Hyg^R; *ΔcsoR::hyg*	This work

CDC1551:

CDC1551	WT	W. Bishai collection
JHU0847-269	Kan^R; *ricR::*ΦMycoMarT7	TARGET, Johns Hopkins School of Medicine
MHD588	Hyg^R; WT, pMV306	This work
MHD589	Kan^R, Hyg^R; *ricR::*ΦMycoMarT7, pMV306	This work
MHD590	Kan^R, Hyg^R; *ricR::*ΦMycoMarT7, pMV-*ricR*	This work

***E. coli* strains:**

DH5α	F-, p80d*lacZ*ΔM15 Δ(*lacZYA-argF*)U169 *deoR recA1 endA1*	Gibco, BRL
	hsdR17 (r_k-m_k+) *phoA supE44* λ- *thi-1 gyrA96 relA1*	
ER2566	F- λ- *fhuA2* [lon] *ompT lacZ::T7 gene1 gal sulA11*	(Chong *et al.*, 1994)
	Δ(*mcrC-mrr*)114::IS10 R(*mcr-73*::miniTn10)2	
	R(*zgb-210*::Tn10)(Tets) *endA1* [dcm]	

Plasmids:

pET24b(+)	Kan^r; for production of C-terminal His_6 epitope-tagged protein	Novagen
pET24b(+)-*ricR*	Kan^r; for expression of *ricR*-his_6	This work

pET24b(+)-*ricR*-stop	Kan^r; for expression of un-tagged *ricR*	This work
pET24b(+)-*csoR*	Kan^r; for expression of *csoR*-his$_6$	This work
pMV306	Hyg^r; integrates in single copy on the chromosome	(Stover et al., 1991)
pMV306-*pafA*	Hyg^r; for complementation of the *pafA* mutant	(Festa et al., 2007)
pMV306-*mpa*	Hyg^r; for complementation of the *mpa* mutant	(Darwin et al., 2003)
pMV306-*ricR*	Hyg^r; for complementation of the *ricR* mutant	This work
pYUB-*csoR*	Hyg^r; 700 bp flanks of *csoR* cloned on either end of a hyg^r cassette	This work
pAJD107	Amp^r; large multiple cloning site	(Darwin & Miller, 2001)
pAJD-*lpqSp*-GG-TT	Amp^r; plasmid with the *lpqS* promoter cloned, GG to TT mutation	This work
pAJD-*lpqSp*-Destroy	Amp^r; plasmid with the *lpqS* promoter cloned, palindrome is destroyed	This work
pYUB854	Hyg^r; allelic exchange vector	(Bardarov *et al.*, 2002)

Primers:

Rv2963 RACE1	GTTGGCGGTCCAATAATGAT
Rv2963 RACE2	GACCTGGGAAATCCTGTGG
lpqS PE	TTTGGGTGAGCCACATGAC
mymT RACE1	CTACTTGACCGGGGCCAATTCG
mymT RACE2	CCAATTCGTCGCCGCAGGTGCAG

socA RACE1	TTGAGAATTGCGTCACATCC
socB RACE2	CCATGGAGGGCAAATGTC
Rv0190 RACE1	AGTGGCTCAGGTGCTCGT
Rv0190 RACE2	GCGCTGATCTGGGTCAGAA
Rv2963 qRTF	TTTGGCTCGGTCACTATTCC
Rv2963 qRTR	ATCATTATTGGACCGCCAAC
lpqS qRTF	CTCCCCCAGCTCCACCGTCA
lpqS qRTR	GGTCGGTAAGCGCGGCTGTC
mymT qRTF	AGGGTGATACGAATGACGAAC
mymT qRTR	TCACGTCTACTTGACCGGG
mysT qRTF	CGACCCCGACGAAGTAAGAG
mysT qRTR	GTAGTGCCCAGGCATTGAGA
mysU qRTF	CTGAAAGCCCGGAAGGA
mysU qRTR	TCACGTAACGCCCTGAGC
Rv0190 qRTF	CTACACGCAGCAAAAGGACA
Rv0190 qRTR	GTGCTCGTCCAGCAGGTT
rpoB qRTF	TCGTTCTCTGACCCTCGTTTC
rpoB qRTR	ACGTGCCCTTCTCGGTCATCA
csoR qRTF	AAGGAATTGACCGCAAAGAA

csoR qRTR	CACGTCTCCAAGTGGTTGTG
ctpV qRTF	CGCGTGTGCGTCACCGGG
ctpV qRTR	CCGACAGCACGGCGGCGG
dlaT qRTF	ACAACGAGGACACCAAGGAG
dlaT qRTR	TACCGATGTTGGTGATGGG
Rv0190 comp F-HindIII	GACAAGCTTCATTGTTCAAGTATGCGGCCCAAG
Rv0190 comp R-KpnI	GACGGTACCTCAGGAACGAACCAGGCGCGCG
lpqS affinity F-BIO	[BIO-TEG]ATCGCTCCTCGTCTGGATTT
lpqS affinity R	AGCGCGACCGCGACAATC
pks12 DAC F BIO	[BIO-TEG]GAGCAAGGGTAAGTGGGACA
pks12 DAC R	TCTTGCCCATCTCCAAGAAC
csoR DAC F BIO	[BIO-TEG]CTCATCGTCCACGAGCCTAC
csoR DAC R	AATTCCTTGCTCATGGCTTG
Rv0190 rev stop EcoRI	GACGAATTCTCAGGAACGAACCAGGCGCGCGATTG
RV0190 F NndeI	GACCATATGACAGCAGCACACGGCTACAC
Rv0190 rev XhoI	GACCTCGAGGGAACGAACCAGGCGCGCGATTG
gg1213ttF	CACCCTACCCCTATAGTTTATATAGTGGGCCACGTGGAAG
gg1213ttR	CTATATAAACTATAGGGGTAGGGTGTAAGGGCGGATGATGG
pal destroy F	CACCCCGAGATGATTACGGATATAGTGGGCCACGTGGAAAG

pal destroy R	CTATATCCGTAATCATCTCGGGGTGTAAGGGCGGATGATGG
lpqSIFUPPstI	GACCTGCAGTGGCTCAGTCGGATCGTCGACGAC
lpqS-his6R PstI	GACCTGCAGTCAGTGGTGGTGGTGGTGGTGGCGACGAGCCAGGCAGAAC
csoR KO1 kpnI	GATGGTACCCTTGCTATTTGCGGCTATTTG
csoR KO2 xbaI	GATTCTAGACATGGCTTGCCCCTAATCCCTC
csoR KO3 ncoI	GATCCATGGTGACGAGCGCCGGACTCCG
csoR KO4 hindIII	GATAAGCTTGCAACGCGACGCCTTCAG

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